REMARKS

Claims 1 and 9 have been amended. Claim 61 has been canceled without prejudice. No new matter has been introduced by these amendments. The following addresses the substance of the Office Action.

Priority/written description/new matter

The Examiner has maintained the rejection of Claims 1, 7-9, 60, and 61 under 35 USC §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges that claims 1, 7-9, 60 and 61 are only entitled to a filing date of the present application (10 December 2000). The Examiner believes that although the prior specifications describe polynucleotides encoding a polypeptide comprising SEQ ID NO: 2, they do not describe the far broader genus of polynucleotides encoding polypeptides comprising SEQ ID NO: 41. The Examiner also contends that this language does not find support in the present specification, and considers it to be new matter.

Applicant wishes to note that this application is the US National Phase of a PCT Application with an international filing date of December 15, 1998. Thus, even if the present claims were limited to the filing date of the present application, that filing date would be December 15, 1998.

The Written Description Guidelines (Example 14) acknowledge that a claim directed to homologues having "at least 95% sequence identity" to a specific sequence and having a specific activity is generally supported by a description of that specific sequence. Claims 1 and 9 have been amended to recite that the polynucleotide has at least 95% sequence identity with the polynucleotide encoding the polypeptide comprising SEQ ID NO: 2. Support for this amendment can be found in the PCT application as filed (page 9, lines 13-19), as well as in the priority application No. GB 9726539.1, filed December 16, 1997 (page 9, lines 19-25) (see also Substitute Specification as filed June 3, 2005, on page 9, lines 6-12). Both specifications define variants of the polynucleotide of the invention as having relatively short stretches having preferably at least 95% homology (i.e. 95% identity) with equivalent stretches of the polynucleotide of the invention even though the overall homology between the two polynucleotides may be much less. Thus, one of ordinary skill in the art would recognize that the overall percent identity may also be as high as at least 95%. Furthermore, the functional assay allowing the determination of the migration stimulation factor activity of the polypeptide

encoded by the claimed polynucleotide is well known in the prior art and is described in detail in Gray et al. (1989 *PNAS USA* 86:2438-2442) cited in the Specification as filed and incidentally co-authored by the present inventors, as well as in Picardo et al. (1991 *Lancet* 337:130-133), also cited in the Specification as filed.

Therefore, just as in Example 14 of the Written Description Guidelines, here there is actual reduction to practice of the single disclosed species. The Specification indicates that the genus of nucleic acids encodes the genus of proteins that must be variants of SEQ ID NO: 2 which do not have substantial variation since all of the variants must possess the specified activity, and all members of the genus of the nucleic acids have at least 95% identity to the disclosed species. Therefore, the disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description of the claimed invention.

Therefore, currently amended Claims 1, 7-9, and 60 are fully supported by the Specification of priority application GB 9726539.1 as filed on December 16, 1997 (page 9, lines 19-25, and page 23, lines 20 and 25-26), and they do not contain new matter.

The Examiner further required that the Applicant points to specific passages in the Specification which support the limitation regarding polypeptides having at least 30% of the ability of a polypeptide comprising SEQ ID NO: 2 to stimulate migration of adult skin fibroblasts into a collagen gel. Support for such limitation can be found in the PCT application as filed on page 10, lines 15-17, page 20, lines 25-26 (see also Substitute Specification of the present application at page 10, lines 7-9, and page 20, lines 6-7).

In conclusion, currently amended Claims 1, 7-9, and 60 are fully supported by the Specification as filed and their rejection under 35 USC §112, first paragraph should be withdrawn.

Enablement

The Examiner has maintained the rejection of Claims 1, 7-9, 60, and 61 under 35 USC §112, first paragraph, as non-enabled, because the Specification does not describe an association between SEQ ID NO: 2 and the ability of a polypeptide comprising this amino acid sequence to stimulate migration of adult skin fibroblasts into a collagen gel, and the skilled artisan cannot predict which of the polypeptides comprising SEQ ID NO: 2 might have such activity.

> "To be enabling, the specification of a patent must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' ... Nothing more than objective enablement is required, and

> therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *See In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993).

In the present case, the skilled artisan does not have to rely on predictions or undue experimentation. The Specification recites several passages establishing that a method of detecting migration stimulation factor activity of a polypeptide was known in the art at the time this invention was made (see, e.g. Gray et al. 1989 *PNAS USA* 86:2348-2442; and Picardo et al. 1991 *Lancet* 337:130-133). Therefore a skilled artisan armed with this knowledge will be able to experimentally test any number of polypeptides as described in Claim 1. Such experimentation would be far from undue or unreasonable as nothing more than carrying out the well-known experimental procedures would be required.

Therefore, Applicant asserts that currently amended Claims 1, 7-9, and 60 are fully enabled by the Specification as filed, and their rejection under 35 USC §112, first paragraph should be withdrawn.

Non-obviousness

The Examiner has maintained the rejection of Claims 1, 7-9, 60 and 61 under 35 USC §103(a) as being allegedly unpatentable over Grey et al. (1989 *PNAS USA* **86**:2438-2442), as evidenced by Schor et al. (*Breast Cancer Res.* 2001 **3**:373-379), GenBank™ Accession No. AJ276395, and UniProtKB/SwissProt™ Accession No. P02751, in view of Bendig (of record). Specifically, the Examiner has maintained that the 70 kDa polypeptide designated "MSF", which was isolated from cultured fibroblasts by Grey et al. is the polypeptide of SEQ ID NO: 2. Therefore, because Grey et al. indicated making efforts directed toward cloning the gene for MSF and obtaining its complete sequence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned a nucleic acid molecule encoding the polypeptide isolated by Grey et al. because the methodology to do so was well within the skill of the artisan of ordinary skill at the time the invention was made. The Examiner further stated that there would have been at least a reasonable expectation of success in isolating a nucleic acid molecule encoding a polypeptide comprising SEQ ID NO: 2.

> To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Here, the cited art either taken alone or in combination, fails to provide the required factors. Grey et al. does not disclose any sequences. GenBank™ Accession No. AJ276395 protein sequence was submitted by the inventor on March 6, 2000, which is after the priority date of the present application, and thus does not constitute prior art. UniProtKB/SwissProt™ Accession No. P02751 sequence is that of a fibronectin precursor protein which does not comprise the SEQ ID NO: 41. While the combination of cited references provides a motivation to obtain the polynucleotide sequences as well as a reasonable expectation of success of eventually obtaining them, there is not prediction in the cited art of what these sequences would be. Based of the sequence of fibronectin precursor or the functional characteristics of the purified MSF of Gray there was no way to predict that the recombinant polynucleotide sequence would encode *inter alia* the amino acid sequence of SEQ ID NO: 41.

Furthermore, as discussed previously, *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993) and *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995) are directly analogous to the present claims.

In *Deuel*, the Federal Circuit reaffirmed the principle, stated in *Bell*, that the existence of the general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs (see 1215, right column). The Federal Circuit has also clearly promulgated that the disclosure of a polypeptide sequence does not render obvious the polynucleotide which encodes it. In the present application, there was no disclosure of any polypeptide sequence comprising SEQ ID NO: 41 in the prior art before the inventors discovered it. Therefore, the polynucleotide sequence encoding it is not obvious. Furthermore, the presently claimed invention is not a method of obtaining a DNA sequence based on the possession of a purified protein and methods of sequencing it or methods of cloning a gene for it. The claimed invention is a composition of matter having a specific sequence that the present inventors were the very first ones to discover.

The Examiner further cited *Enzo Biochem Inc. v. Calgene Inc.* (52 USPQ2d 1129, 1138n. 10, Fed. Cir. 1999) in support of the reasoning why he believes that the case law which has not been overturned by the Federal Circuit was not relied upon by the Examiner. However, Enzo is irrelevant for this case as the sequence of an isolated recombinant polynucleotide encoding an amino acid sequence unknown in the prior art is unpredictable. For all the above reasons, Applicant asserts that a *prima facie* showing obviousness cannot be maintained.

Novelty

The Examiner has rejected Claims 1, 7-9, 60 and 61 under 35 USC §102(b) as being allegedly anticipated by WO 99/31233A1. This document is the publication of the international application No. PCT/GB98/03766, of which the present application is a US National Stage. As discussed above, the claimed invention is fully supported by the specification as filed internationally. Therefore, this publication does not constitute prior art for the presently claimed invention.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: September 21, 2006

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